PCCA Lipoderm®

A Compounded Topical Pain Cream for Wrist Osteoarthritis

SUMMARY: Osteoarthritis of the wrist is a common chronic condition that causes musculoskeletal pain and functional disability. The purpose of this case study is to evaluate the effectiveness of a topical cream containing ketoprofen in Lipoderm® in managing wrist pain and improving functionality in a patient. The Patient Specific Functional Scale (PSFS) and a visual analogue scale for pain were used to measure the clinical outcomes. The patient reported decreased pain VAS from 8 to 2 as well as an improvement of PSFS score from 2.5 to 8.6 after use, and the effectiveness has been maintained by daily application. This case study demonstrates the effectiveness and safety of this compounded formulation for pain management in a patient with osteoarthritis.

Introduction:

Osteoarthritis of the wrist, or wrist arthritis, develops due to wearing and narrowing of the articular cartilage between the radius and the scaphoid, leading to pain and stiffness of the wrist. The prevalence is around 10% in general population but is higher in physically demanding occupations and sports.[1] Patients with wrist arthritis often experience swelling, loss of range of motion, weakness and pain during activities.

The management of osteoarthritis of the wrist is similar to the treatment of other joints and the goal is to control pain. If patients do not respond to the first-line nonpharmacological exercise or activity modification, topical nonsteroidal anti-inflammatory drugs (NSAIDs) rather than oral NSAIDs are always recommended due to comparable effectiveness and better safety profile with topical NSAIDs.[2] The most studied NSAIDs for osteoarthritis are diclofenac and ketoprofen. Diclofenac gel is FDA approved and available in 1% to 3% strength, while ketoprofen is commercially available in the U.S. only as oral capsules. A higher dose of diclofenac gel or a topical form of ketoprofen can be prescribed and compounded by extemporaneous compounding according to individual patient needs. Topical capsaicin is also used for wrist arthritis sometimes but is not preferred over NSAIDs because of less evidence of efficacy and poorer tolerability.[2] Alternative treatments include duloxetine, intraarticular glucocorticoid injection and surgery if no symptom relief is received from topical therapy.[2] The alternatives are either with more adverse effects, short duration of action, or invasive procedure, and are always reserved as last-line therapies. Therefore, effective and safe topical therapies are desired to improve symptoms and restore wrist function to prevent patients from more aggressive treatments.

The purpose of this case study is to present the effectiveness of a compounded topical formulation (Table 1.) in reducing pain and improving wrist function in a patient with wrist arthritis.

Rx	
Ketoprofen USP, PCCA Special Micronized	10%
Cetyl Myristoleate (CMO) 20% (Powder)	4%
Ethoxy Digycol Reagent	5%
Base, PCCA Lipoderm®	q.s.

Table 1. The compounded Ketoprofen 10% Topical Lipoderm formulation for wrist arthritis (PCCA F13720).

Methodology:

The Patient Specific Functional Scale (PSFS) was implemented to quantify the impact arthritis pain has on how the patient perform certain activities before and after using the compounded formulation. The PSFS is a self-report functional assessment scale that focuses on the activities that are important in the patient's daily life but they are unable to do or have difficulty performing due to chronic pain.[3] During the initial assessment before treatment, the patient was asked to identify up to five activities that are important in his daily life but were impaired by the wrist arthritis pain, and also rate the current level of difficulty associated with each activity on an 11-point scale. The patient was then followed up on the day after first application, one month and two months afterwards. During each follow-up, the patient was asked again to rate the activities previously identified and add new problematic activities if there were any. On the 11-point scale, the minimum score of "0" represents "unable to perform the activity," while a maximum score of "10" represents "able to perform the activity at the same level as before injury or problem." When calculating the total activity score, the sum of the score from each activity was divided by the number of activities. Therefore, the total activity score ranges from 0 to 10, indicating the activity level from the most impaired to the least impaired. In addition, the patient was also asked to score the overall pain level on a 1-10 Visual Analogue Scale (VAS), in which a higher score correlates with more severe pain. Adverse effects from the topical therapy were also evaluated during follow-ups.

Written informed consent was obtained from the patient for publication of this case study.

Case Report:

Patient BW is a 69-year-old male with osteoarthritis in the right wrist for many years. BW was a law enforcement officer and hand/wrist activities were heavily involved in his daily job, such as the use of a handgun and tools, but the wrist pain increased while performing these activities in recent years. BW used to spend a lot of time fishing after work, but started to complain about the difficulties when casting a fishing rod, paddling a kayak and catching fish due to enhanced pain. Prior to the compounded pain cream, BW was prescribed diclofenac topical gel 1% and 3%, but reported no noted improvement. He then was instructed to apply the compounded topical pain cream twice daily to the wrist and 30 minutes before intense hand activities, such as shooting and fishing.

Since BW had not complained about performing daily living activities, instead, he was more concerned about the hand activities involved in his job duties and his hobby of fishing, the PSFS was selected to be one of the outcome measurements. BW identified his five most concerning activities as: using a screwdriver, casting a rod and retrieving fish during fishing, pushing up on his hands, using garden tools and using a handgun. Before using the topical pain cream, BW scored each of these initial activity levels ranging from 1 to 3, meaning he had significant difficulty performing them. The baseline VAS pain score was 8, which was severe.

The patient reported relief of pain 30 minutes after first application of the cream and reduction of swelling after two days.

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With the twice daily maintenance dose and the rescue dose 30 minutes before heavy activities, BW reported that the level of all activities improved significantly and he achieved an average score of 8.6, which was close to his original levels, and his pain score reduced to 2, which was improved from severe to mild pain (Figure 1). The effect of the compounded pain cream lasted throughout the study period.

The patient reported no adverse reaction associated with the topical treatment.

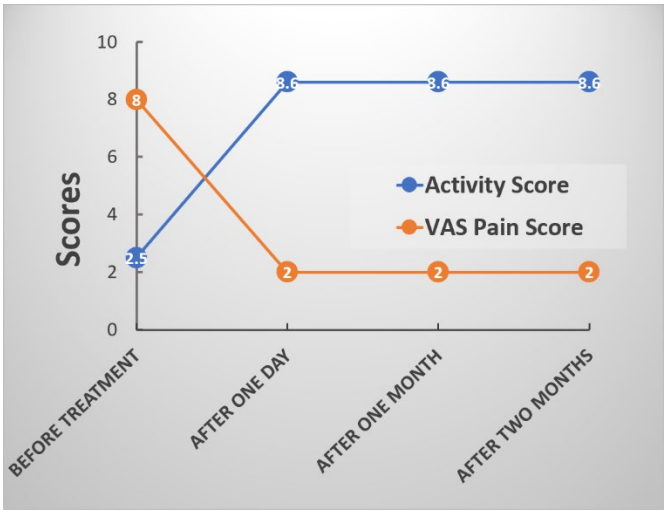

Figure 1. The clinical outcomes of treatment with Ketoprofen 10% topical pain cream. The activity score obtained from PSFS and the VAS pain score before treatment, one day, one month and two months after first application were presented. High activity score means less impaired activity level, while lower VAS pain score indicates lower level of pain.

Discussion and Conclusions:

Wrist osteoarthritis is a common chronic condition that can significantly impair hand function and cause disability. Despite osteoarthritis being previously classified as noninflammatory arthritis, more and more evidence has revealed the involvement of inflammatory cytokines in patient serum and synovial fluid, and the role of chronic inflammation has begun to be recognized.[4] No current treatment can prevent or stop the progression of the disease, but the focus is to control pain and restore wrist function. Topical NSAIDs have been widely used but the effectiveness is not consistent, largely due to the limited drug penetration to the inflamed joint and muscle tissue from topical application. Here we present a potentially effective therapeutic strategy incorporating a commonly used oral NSAID into a topical cream, from which the agent is delivered into skin and underlying joint and tissues to relieve symptoms of osteoarthritis.

Ketoprofen exerts its anti-inflammatory effect through inhibiting cyclooxygenase-2 (COX-2) and decreasing proinflammatory cytokines. Multiple clinical trials have proven the efficacy and safety of topical ketoprofen for osteoarthritis and it has a better safety profile than topical diclofenac.[5] The patient in this case previously failed using 3% diclofenac, so switching to ketoprofen and increasing the dose is a reasonable approach. Topical ketoprofen at 10% has been shown to have good local tolerability and satisfied clinical outcomes,[6] thus was included in this formulation to ensure sufficient drug delivery to the inflammatory site.

There are two excipients in this formulation. Cetyl myristoleate (CMO), a cetylated fatty acid, is used as an emollient, and ethoxy digycol is the wetting agent. Additionally, a penetration-enhancing vehicle allowing prolonged and steady drug permeation through the skin to the pain site is also critical to ensure therapeutic effect. Lipoderm, the penetration-enhancing base used in this formulation, is a phospholipid emulsion system with permeation enhancers that facilitate drug across stratum corneum and entering cutaneous circulation with a prolonged and steady flux rate. The capability of Lipoderm and the kinetics of ketoprofen permeation have been published.[7]

As a result, this compounded formulation successfully reduced pain and swelling, and restored hand function in this patient. The reported therapeutic strategy may provide a flexible, convenient, effective and safe option for future joint osteoarthritis management.

References:

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